

Epidemiology of hepatitis B in Canada

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J Zhang, S Zou, A Giulivi. Epidemiology of hepatitis B in Canada. *Can J Infect Dis* 2001;12(6):345-350.

OBJECTIVE: To provide a current and comprehensive review of the epidemiology of hepatitis B virus (HBV) in Canada.

DATA SOURCES: Published and unpublished epidemiological studies and surveillance reports of the past decade, primarily from Canada were studied. Fifty reports addressing HBV surveillance, incidence and prevalence, transmission-associated risk factors, co-infections, and prevention strategies were reviewed.

DATA SYNTHESIS: HBV infection is an important vaccine-preventable infectious disease in Canada. The incidence rate of clinically recognized, acute HBV infection in 1998/1999 was estimated to be 2.3/100,000 people or approximately 700 cases a year. The prevalence of HBV carriers is estimated to be 0.5% to 1.0% of the population, but varies substantially according to population-specific risk factors. Most acute HBV infections are associated with injection drug use or high risk heterosexual activities, but 20% to 30% of acute cases did not report any identified risk factors. Surveillance activities such as the National Notifiable Disease Reporting system provide information regarding trends and risk factors. The primary preventive strategy for HBV consists of universal immunization for preadolescents and/or infants. Other strategies, such as the universal prenatal screening and postnatal immunization, and the prevention of nosocomial acquisition, are also important. The recently described hepatitis B surface antigen (HBsAg) escape mutants may not be detected by current HBsAg test assays, and the existing HBV vaccines may not protect vaccinees from infections by such mutants.

CONCLUSION: Ongoing surveillance and research are required to assess risk factors for HBV transmission, evaluate the effectiveness of immunization programs and monitor the impact of HBsAg escape mutants.

Key Words: *Canada; Epidemiology; Hepatitis B; Prevention; Risk factors; Surveillance*

Épidémiologie de l'hépatite B au Canada

OBJECTIF : Faire le point de façon globale sur l'épidémiologie de l'hépatite B au Canada.

SOURCES DES DONNÉES : Études épidémiologiques publiées et non publiées et rapports épidémiologiques des dix dernières années principalement au Canada. Cinquante rapports sur l'épidémiologie du HBV, son incidence et sa prévalence, les facteurs de risque de sa transmission, les co-infections et les stratégies de prévention ont été passés en revue.

SYNTHÈSE DES DONNÉES : L'infection au HBV est une importante maladie infectieuse qu'il est possible de prévenir au moyen d'un vaccin. Au Canada, l'incidence de l'infection aiguë au HBV cliniquement reconnue en 1998-1999 a été estimée à 2,3/100 000 personnes ou à approximativement 700 cas par année. La prévalence des porteurs du HBV se situerait à 0,5 - 1 % dans la population, avec une variation substantielle selon les facteurs de risque. La plupart des infections au HBV aiguës sont associées à l'utilisation de drogues par injection ou à des activités hétérosexuelles à haut risque, mais dans 20 à 30 % des cas aigus aucun facteur de risque n'a clairement pu être identifié. Les mesures épidémiologiques comme le système de maladies à déclaration obligatoire offrent des renseignements sur les tendances ou les facteurs de risque. La principale stratégie préventive contre le HBV est l'immunisation universelle des pré-adolescents et/ou des nourrissons. Parmi les autres stratégies tout aussi importantes, mentionnons le dépistage prénatal universel et l'immunisation postnatale, de même que la prévention des infections nosocomiales. Des souches mutantes de l'antigène de surface du virus de l'hépatite B pourraient donc échouer à protéger les sujets vaccinés contre les infections causées par ces souches.

CONCLUSION : Il faut maintenir la surveillance et poursuivre la recherche pour évaluer les facteurs de risque de transmission du HBV, mesurer l'efficacité des programmes d'immunisation et surveiller l'impact des souches mutantes du HBsAg.

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Received for publication November 1, 2000. Accepted August 28, 2001

Hepatitis B virus (HBV) infection is a major public health problem. In 1998, 970 HBV cases were reported in Canada through the National Notifiable Disease Reporting (NNDR) system, the third highest number of cases among reportable vaccine preventable diseases (1). The prevalence of chronic hepatitis B surface antigen (HBsAg)-positive carriers among Canadians is estimated to be 0.5% to 1.0% but has been shown to vary according to ethnicity, occupation and other risk factors (2).

Acute HBV infection is usually asymptomatic among infants and young children (3). Over 95% of infants and 90% of children between the ages of one and five years do not develop symptoms. However, approximately 30% to 50% of adolescents and adults develop clinical symptoms such as jaundice. Age at infection is also one of the most important factors influencing the probability of developing chronic HBV infection. The risk of subsequent chronic HBV infection is about 90% for infants, 25% to 50% for children aged one to five years, 5% to 10% for adolescents, and 1% to 5% for adults. After several decades, 20% to 25% of HbsAg-positive carriers will develop cirrhosis and about 5% to 6% will develop hepatocellular carcinoma (4).

PUBLIC HEALTH SURVEILLANCE OF HBV IN CANADA

NNDR system: HBV infection has been reportable through the NNDR system since 1969, and the responsibility of Health Canada, the Division of Disease Surveillance since 1988 (5). Recently, HBV infection was ranked as the 19th most important infectious disease in Canada (6).

In general, physicians are required to report clinically diagnosed HBV cases (with or without laboratory confirmation) to their local health authority (ie, health unit, regional health department). Cases that meet the HBV surveillance case definition are officially reported to provincial or territorial public health authorities (7). Local laboratories are also required to report laboratory-confirmed HBV cases to provincial laboratories, which then report the cases to both local and provincial or territorial public health authorities.

The case definition of HBV infection has been revised over the years as knowledge has expanded and laboratory tests have improved. The most recent case definition (October 1999) for confirmed acute HBV cases includes: HBsAg positive and immunoglobulin (ig) M antibody to hepatitis B core antigen (HBc) (IgM anti-HBc) positive; or discrete onset of symptoms and jaundice or elevated serum aminotransferase levels and HBsAg positive (and antihepatitis A virus [HAV] and antihepatitis C virus [HCV] negative) when the test for IgM anti-HBc is not available; or loss of HBsAg over six months in the context of a compatible clinical history or probable exposure (8). Diagnosis-associated misclassification may occur because chronic HBV-infected individuals who are sometimes IgM anti-HBc positive and they can also have flares of clinical disease that may mimic an acute infection.

Aggregate data on HBV infections from each province and territory are sent to Health Canada on a monthly basis.

However, reporting practices across jurisdictions remain inconsistent because some jurisdictions report only acute HBV cases, while others report acute and indeterminate HBV cases together, and efforts to investigate and remove duplicate HBV cases vary across jurisdictions. Due to the changes in case definition over the years and inconsistent reporting practices, the cases reported to NNDR system probably include both acute and prevalent cases, and therefore, cannot be used for HBV incidence calculations. In addition, risk factor information is not collected, and the case-by-case reporting carried out by some provinces and territories does not contain standardized data elements. Although the current NNDR system provides valuable data, further standardization is required to meet the public health surveillance needs for HBV infection in Canada.

Enhanced surveillance for HBV: To address the surveillance needs and the information gaps identified above, an enhanced surveillance system for HBV and HCV was established in six health units (one province and five health regions – New Brunswick, Ottawa-Carleton, Winnipeg, Calgary, Edmonton and Vancouver-Richmond) in Canada, with a total population of approximately 4.6 million people. The objectives were to identify and interview all acute HBV cases to estimate the incidence and monitor trends of acute HBV infection; to examine risk factors associated with transmission of acute HBV infection; and to evaluate the effectiveness of preventive programs.

The surveillance methods and operating procedures have been described in detail elsewhere (9). Briefly, a consensus protocol, and standardized case definitions and questionnaires were developed, and were used by all six health units. Information on demographic factors, clinical characteristics and laboratory testing results were collected through contact with physicians and laboratories, while information on potential risk factors are obtained from telephone interviews of each cases. Data from each health unit are sent to Health Canada on a monthly basis for analysis of incidence rate and risk factors.

Targeted surveillance and research: The Canadian Needlestick Surveillance Network (CNSSN) was established in 1998 by Health Canada in collaboration with provincial, territorial and regional health authorities, and hospitals across the country (personal communication, Onno Sharon). The purpose of this surveillance network is to collect surveillance data from a representative sample of health care facilities to estimate the magnitude of occupational bloodborne seroconversion, as well as the morbidity, mortality and the economic burden of HBV and HCV infection among health care workers (HCWs). A standardized protocol and software package for data collection are used by participants to investigate and follow-up needlestick injuries among HCWs. The data include demographic characteristics, job title, nature of blood or fluid exposures, source of the exposure and outcomes. This information is sent to Health Canada for analysis. Information generated from this surveillance network will support evidence-based decision-making regarding the

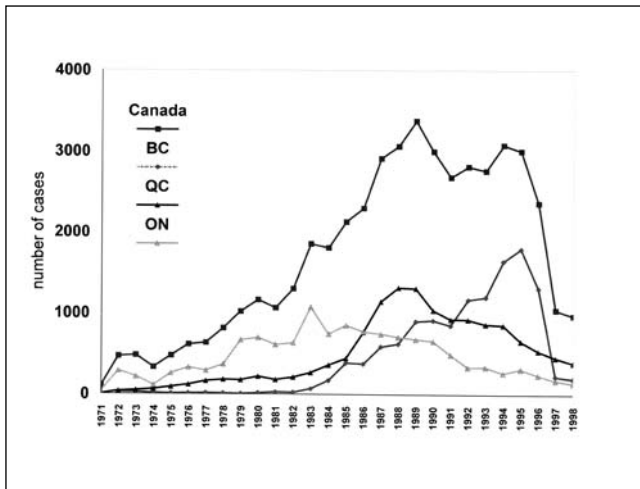


Figure 1) Reported hepatitis cases in Canada from the National Notifiable Disease Reporting system from 1971 to 1998. BC British Columbia; ON Ontario; QC Quebec

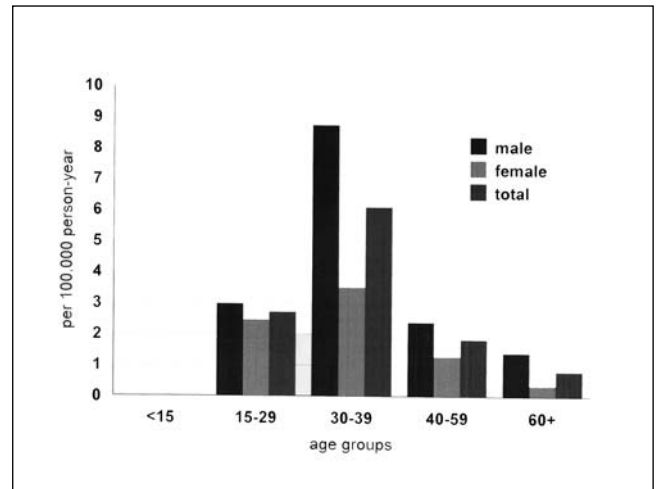


Figure 2) Estimated acute hepatitis B virus infection incidence rates from enhanced surveillance of hepatitis B virus in four health regions in Canada, 1998 to 1999

prevention of bloodborne pathogen infections among HCWs.

In addition to surveillance activities, selected epidemiological studies focusing on HBV have been carried out in Canada to address specific research questions. These include the evaluation of the effectiveness of HBV immunization programs, examination of unknown risk factors and assessment of the magnitude of known risk factors.

Recently, research attention has been turned to the examination of HBsAg escape mutants. These have mutations at amino acid 124 to 147 of HBsAg and may not be detected by current HBsAg test assays (10). The existing HBV vaccines also may not protect vaccinees from infections by these mutants (11). Immune pressure from vaccination against HBV may induce the occurrence or selection of HBsAg mutations (12). Due to the potential impact of these mutants on HBV prevention and control, research activities have been proposed, including the evaluation of the prevalence of mutant infections in the Canadian population, identification of risk factors associated with mutant development and assessment of implication of these mutants for the safety of the blood system.

PREVALENCE AND INCIDENCE OF HBV IN CANADA

Data from the NNDR: The number of reported HBV cases in Canada has increased considerably since 1971, peaking in 1989 ($n=3378$), fluctuating from 1990 to 1995 and dropping dramatically thereafter (Figure 1). The increasing number of reported cases between 1971 and 1989 may be due to better reporting of and testing for HBV, a rise in injection drug use and an increased number of immigrants from endemic regions. On the other hand, the significant decline of reported HBV cases in 1997 may be related to the change in HBV-reporting practice in British Columbia in that year.

Incidence and prevalence: Due to limitations of the NNDR data, HBV incidence rates in Canada cannot be calculated directly from the reported number of HBV cases. After the removal of nonacute cases through inquiries to provincial

and territorial epidemiologists (13), the estimated rates of acute HBV infection showed a decrease from 5.0 to 3.5/100,000 population between 1992 and 1995. In 1998/99, the incidence of acute HBV infection was estimated to be approximately 2.3/100,000 population (Figure 2) (9).

The prevalence of HBsAg-positive carriers is lowest in the general population; intermediate in the Aboriginal population, adolescents, sexually transmitted disease clinic visitors and residents of long term care facilities; and highest in the Inuit population and immigrant populations from Southeast Asia and Africa. The HBsAg-positive rate has been reported to be 0.4% for preadolescents, 0.3% for sexually transmitted disease clinic visitors and 0.6% for residents of long term care facilities (14-17). About 26.4% of the Inuit population demonstrates evidence of previous HBV infection (anti-HBc positive) and 6.9% are HBsAg positive (18). The prevalence of HBsAg-positive carriers was 0.3% in Aboriginal persons, with 11.3% having evidence of previous HBV infection (19). Among pregnant women, the prevalence was 7.4% for those born in Asia and 0.1% for those born in Canada (20,21). Immigrants from Southeast Asia who were HBsAg positive were more likely to be hepatitis B e antigen (HBeAg)-positive (50%) than those in the Aboriginal population (8.8%) (22,23).

RISK FACTORS FOR TRANSMISSION OF HBV IN CANADA

HBV is transmissible through several routes (24-27): percutaneous – injection drug use, exposures to contaminated blood or bodily fluids; sexual – heterosexual or male homosexual activities; vertical – from mother to infant; and horizontal – among children and household contacts.

Injection drug use and high risk heterosexual activities are the major risk factors associated with HBV transmission in Canada (9,16,28). Increasing years of sexual activity, multiple sexual partners and sex with HBeAg-positive carriers were associated with an elevated risk (29). Homosexual activities, tattooing and body piercing, having an HBsAg car-

rier in the family, and a history of blood transfusion also increase the risk of HBV infection among Canadians (9,29,30).

COINFECTION OF HBV AND OTHER VIRUSES

Coinfection of HBV with other bloodborne pathogens, such as HCV, hepatitis delta virus and HIV, may affect the natural history and clinical severity of HBV infection. HBV-HCV coinfection among injection drug users seems to increase the severity of chronic HBV infection outcomes, especially the risk of hepatocellular carcinoma (31). One study reported that chronic HBV or HCV infection increased the risk by a factor of 28.8 and 31.2, respectively, and that coinfection of HBV-HCV increased the risk by a factor of 42.9 (32). Hepatitis delta virus infection among HBV-infected individuals, not only increases the severity of acute HBV infection and the risk of fulminant HBV infection, but also increases the risk of becoming a chronic carrier and the severity of chronic HBV infection outcomes. Injection drug users coinfecting with HIV and HBV were more likely to be asymptomatic, but also more likely to become chronic HBV carriers (31). Coinfection with HAV among HBV carriers often leads to fulminant hepatitis. Therefore, HAV immunization for chronic HBV carriers is recommended. The prevalence of these coinfections among Canadians is largely unknown.

PREVENTION OF HEPATITIS B IN CANADA

Interventions to prevent HBV infections in Canada have been developed and implemented through various federal, provincial and territorial programs or initiatives. These include the prevention of vertical HBV transmission, the prevention of nosocomial HBV transmission, HBV immunization, blood and organ donor screening, and public health response.

Prevention of vertically transmitted HBV: Vertical transmission is not a major route of HBV acquisition in Canada. However, in the absence of prenatal screening and postnatal immunization, about 80% to 90% of babies born to HBeAg-positive mothers will be infected with HBV, and more than 85% of them will become chronic HBsAg carriers. Among babies born to HBsAg-positive but HBeAg-negative mothers, about 2% to 15% will be infected, and 10% to 15% of the infected babies will become chronic carriers (33). The majority of these babies (more than 90%) are infected during or immediately after delivery, and became HBsAg positive within six months. Women who have acute HBV infection in the first or second trimester rarely transmit HBV to their babies. The risk of vertical transmission is increased up to 70% if the acute HBV infection occurs during the last trimester of pregnancy (34).

To prevent vertical HBV transmission, all pregnant women in Canada are tested for HBsAg during prenatal visits or at the time of delivery. Infants born to HBV-infected mothers should receive hepatitis B immune globulin (HBIG) within 48 h after birth and a course of three doses of HBV vaccine within six months after birth (35). The administration of HBIG and HBV vaccine reduces the risk of vertical transmission by over 90%, and less than 5% of the remaining infected

infants becomes chronic carriers (34). However, these strategies may fail to prevent vertical transmission in some cases (33). These include the 2% to 10% of infected infants who acquire HBV infection in utero; those with a high maternal HBV-DNA level; those with an inadequate active antibody response to the vaccine; or those with HBsAg-mutant infection which may not be prevented by HBV vaccination.

Prevention of nosocomial transmission of HBV: The incidence of HBV among HCWs was as high as 50 to 120/100,000 population in the 1970s to the early 1980s (36). In the absence of immunization for HCWs, the risk of HBV infection following an HBV-positive needlestick or sharps injury was estimated to be 2% to 40%, with a narrow range of 15% to 30% (37,38). The risk was higher (19% to 30%) for HCWs exposed to HBeAg-positive blood than for those who were exposed to HBeAg-negative blood (5%) (36). The risk has decreased dramatically over the past 20 years as a result of the HBV vaccination of HCWs and increased attention to preventing sharps injuries. Comprehensive prevention and control guidelines have been developed in Canada to prevent HBV transmission from patients to HCWs, from patients to patients and from HCWs to patients (39).

HBV immunization: In Canada, HBV vaccination is recommended for all individuals who are at increased risk of HBV infection (35). This strategy has several limitations. Risk factors cannot be identified for about 30% of HBV cases (9); there is poor compliance to the HBV vaccine schedule in high risk groups (40,41); and HBV infections occur at early stages of intravenous drug use before individuals are identified as being at risk (31).

The Canadian Hepatitis B Working Group recommended a universal HBV vaccination program for preadolescents (35). Since the early 1990s, all provinces and territories have implemented a universal school-based HBV vaccination program targeting preadolescents aged nine to 13 years (42). High completion rates (91% to 93%) have been reported (43). These programs could prevent 63% of acute HBV infections and 47% of the chronic HBV infections in Canada (44). However, without a complementary infant vaccination strategy, chronic HBV infection that occurs in infancy or early childhood, which accounts for 10% to 15% of all chronic infections in Canada, will not be prevented (45). To strengthen immunization programs in Canada, some jurisdictions (including British Columbia, New Brunswick, the Northwest Territories, Prince Edward Island and the Yukon Territory) have undertaken a universal program which combines infant and preadolescent vaccination (42,46,47).

HBV vaccination is safe and effective, and protection can last for at least 15 years (35). The antibody response rate is high in the general population (90% to 95%), but low in immunocompromised individuals (eg, 50% to 70% for persons infected with HIV) (35). These rates may vary with ethnic origin (48). The emergence of HBsAg mutants may have a potential impact on the effectiveness of HBV vaccination.

Other prevention strategies: The current risk of HBV transmission through blood transfusion or organ transplantation

is minimal due to blood or organ donor screening and HBsAg testing. However, residual risk still exists due to a window period (49) and HBsAg-mutant infections (11).

Public health tracing and notification of contacts, with the provision of immunization where indicated, as well as public health education and promotion targeting behaviour changes, may also play an important role in the prevention of HBV infection.

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BOOK REVIEWS

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Viral Infections of the Respiratory Tract (1999). Raphael Dolin, Peter F Wright, eds. Marcel Dekker Inc, New York, New York. ISBN 0-8247-0195-X; 432 pages; US\$185.00

Respiratory tract infections are probably the most common reason that medical attention is sought for both children and adults worldwide. As the ability to diagnose viral respiratory tract infections improves, and new antiviral therapies and immunization products enter the market place, infectious disease specialists will increasingly be asked for advice related to public health, infection control and patient management. A new volume in the monograph series, *Lung Biology in Health and Disease, Viral Infections of the Respiratory Tract* brings together basic and clinical research about many of these viral pathogens and makes superb reading for infectious disease specialists, microbiologists, pulmonologists and public health professionals.

Edited by Drs Peter F Wright and Raphael Dolin, the book has contributions from 16 active and well known investigators, most of whom are clinicians. The volume is divided into five sections: viral infections in different populations (children, adults, older people, immunocompromised patients), specific viruses (influenza A and B, respiratory syncytial viruses [RSV], parainfluenza viruses, adenoviruses, rhinoviruses and coronaviruses, and hantavirus), followed by sections on diagnosis, treatment and prevention.

The volume makes enjoyable reading and serves educational goals. Although it is not entirely consistent, in general, the authors cogently synthesize huge amounts of

information (the chapters on influenza and RSV have 352 and 297 references, respectively). The molecular biology of infection is more detailed than standard texts, as is the microbiological basis for diagnostic testing. The pathophysiology of each viral infection, including immune responses, are clearly explained, with sufficient background explanation to make the topic understandable to those outside the field.

Perhaps for reasons of space or because they are not predominately respiratory viruses, there are no specific chapters devoted to cytomegalovirus, varicella zoster virus and herpes simplex; however, the diagnosis and prevention of these viruses are addressed in other chapters.

The volume is the latest in a series of 126 monographs published since 1973 on lung biology, and is the first to deal with viral infections. The editors state that the goal of the volume is "to direct attention more specifically to viral aspects of respiratory disease in a way that will be useful to those without formal training in infectious disease, and to emphasize the many ways in which viral infections influence respiratory physiology and pathology." It is, therefore, surprising them that there is little reference to the effect of these pathogens on pulmonary function in the short and long term. These shortcomings aside, *Viral Infections of the Respiratory Tract*, is a commendable work and well worth adding to one's personal or institutional library for reference or reading.

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